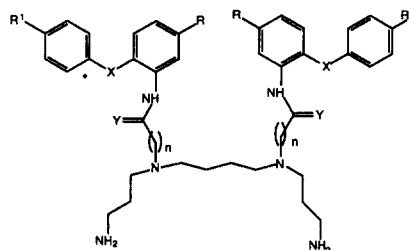


New Spermine and Spermidine Derivatives as Potent Inhibitors of *Trypanosoma cruzi* Trypanothione Reductase

Bioorg. Med. Chem. 1997, 5, 1249

Béatrice Bonnet, David Soulez, Elisabeth Davioud-Charvet, Valérie Landry, Dragos Horvath and Christian Sergheraert*
Laboratoire de Chimie des Biomolécules, URA CNRS 1309, Institut Pasteur, Faculté de Pharmacie, 1 rue du Professeur Calmette, 59019 Lille, France

Several spermine and spermidine derivatives containing 2-amino diphenylsulfide substituents were prepared and tested for their inhibiting effects on *T. cruzi* trypanothione reductase. IC₅₀ values were assessed between 0.3 and 3 μM. Compound **32** (K_i = 0.4 μM) is the most potent TR inhibitor described so far.

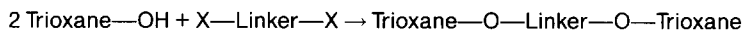


Trioxane Dimers Have Potent Antimalarial, Antiproliferative and Antitumor Activities In Vitro

Bioorg. Med. Chem. 1997, 5, 1257

Gary H. Posner,^{a,*} Poonsakdi Ploypradith,^a Whitney Hapangama,^a Dasong Wang,^a Jared N. Cumming,^a Patrick Dolan,^b Thomas W. Kensler,^b Donna Klinedinst,^c Theresa A. Shapiro,^c Qun Yi Zheng,^d Christopher K. Murray,^{d,*} Lynn G. Pilkington,^d Lalith R. Jayasinghe,^d Jeff F. Bray^d and Randy Daughenbaugh^d
^aDepartment of Chemistry, School of Arts and Sciences, ^bDivision of Toxicological Sciences and The Environmental Health Sciences Center, Department of Environmental Health Sciences, School of Hygiene and Public Health, and ^cDepartment of Medicine, School of Medicine, The Johns Hopkins University, Baltimore, MD 21218, U.S.A. ^dSynthetic Chemistry Research and Development Group, Hauser Chemical Research Co., Inc., 5555 Airport Boulevard, Boulder, CO 80301, U.S.A.

A series of tetracyclic and tricyclic trioxane dimers with ether and ester tethers of varying length and flexibility were prepared and found to have potent and potentially therapeutically valuable antimalarial, antiproliferative, and antitumor activities in vitro.



Identification and Biosynthesis of (E,E)-10,12-Tetradecadienyl Acetate in *Spodoptera littoralis* Female Sex Pheromone Gland

Bioorg. Med. Chem. 1997, 5, 1267

Isabel Navarro, Esther Mas, Gemma Fabriàs* and Francisco Camps
Departament de Química Orgànica Biològica, CID-CSIC, Jordi Girona 18-26, 08034 Barcelona, Spain

A minor component of *Spodoptera littoralis* sex pheromone has been identified as (E,E)-10,12-tetradecadienyl acetate. Mass-labeling experiments showed that the (E,E)-10,12-tetradecadienoyl moiety is biosynthetically derived from (Z)-11-tetradecenoic acid.

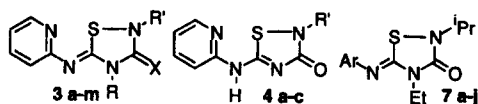


Arylimino-1,2,4-Thiadiazolidinones: A New Family of Potassium Channel Openers

Bioorg. Med. Chem. 1997, 5, 1275

Ana Martínez,^{a,*} Ana Castro,^a Ignacio Cardelús,^b Jesús Llenas^b and José M. Palacios^b
^aInstituto de Química Médica (CSIC), Juan de la Cierva 3, 28006 Madrid, Spain and ^bLaboratorios Almirall S.A., Cardener 68-74, 08024 Barcelona, Spain

The use of thiadiazolopyridinium chlorides as intermediates in heterocyclic synthesis has led to a new class of potassium channel openers.



Galactosylation with β -Galactosidase from Bovine Testes Employing Modified Acceptor Substrates

Bioorg. Med. Chem. 1997, 5, 1285

Ulrike Gambert,^a Raul Gonzalez Lio,^{a,b} Erzsébet Farkas,^{a,c} Joachim Thiem,^a Vicente Verez Bencomo^b and András Lipták^c

^aInstitut für Organische Chemie, Universität Hamburg, Martin-Luther-King-Platz 6, D-20146 Hamburg, Germany

^bFacultad de Química, Universidad de la Habana, Ciudad Habana, 10400, Cuba

^cInstitute of Biochemistry, Lajos Kossuth University, P.O. Box 55, 4010 Debrecen, Hungary

Modified acceptor substrates opened further possibilities for the galactosidase-catalyzed synthesis of bioactive disaccharides using β -galactosidase from bovine testes.



Two Non-Racemic Preparations of a Piperidine-Based NMDA Antagonist with Analgesic Activity

Bioorg. Med. Chem. 1997, 5, 1293

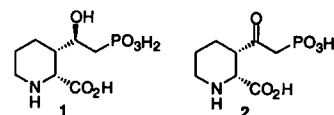
Britt-Marie Swahn,^a Karin M. Edvinsson,[†] Elisabet Kallin,^a Ulf Larsson,^b Odd-Geir Berge,^a Håkan Molin,^a Benjamin Pelcman^a and Alf Claesson^{a,*}

^aPreclinical Research, Astra Pain Control AB, S-15185 Södertälje, Sweden

^bChemical Process Development Laboratory, Astra Production Chemicals AB, S-15185 Södertälje, Sweden

[†]Present address: Medicinal Chemistry, Astra Hässle AB, S-43183 Mölndal, Sweden

The non-racemic preparation of **1** is described. The analgesic effects of (\pm)-**1** and the earlier described (\pm)-**2** were evaluated using the mouse hot-plate test and the mouse formalin model.

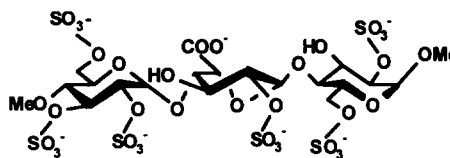


Combined NMR and Molecular Modeling Study of an Iduronic Acid-Containing Trisaccharide Related to Antithrombotic Heparin Fragments

Bioorg. Med. Chem. 1997, 5, 1301

Soizic Cros,^a Maurice Petitou,^b Philippe Sizun,^c Serge Pérez^d and Anne Imberty^{d,*}

^aIngénierie Moléculaire, INRA, BP 1627, 44316 Nantes Cédex 03, France; ^bSANOFI Recherche, 195 route d'Espagne, 31000 Toulouse, France; ^cSANOFI Recherche, 371 rue du Professeur Blayac, 34000 Montpellier, France; and ^dCERMAV-CNRS, BP 53, F-38041 Grenoble Cédex 09, France



The Discovery, Characterization and Crystallographically Determined Binding Mode of an Fmoc-Containing Inhibitor of HIV-1 Protease

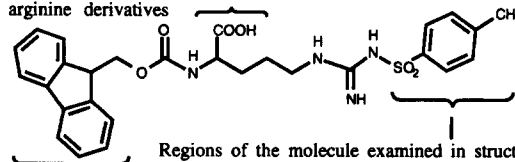
Bioorg. Med. Chem. 1997, 5, 1311

Earl E. Rutenber,^a James J. De Voss,^b Lucas Hoffman,^a Robert M. Stroud,^{a,b} Kwan H. Lee,^b Juan Alvarez,^b Fiona McPhee,^b Charles Craik^{a,b} and Paul R. Ortiz de Montellano^{b,*}

^aDepartment of Biochemistry and Biophysics and

^bDepartment of Pharmaceutical Chemistry, University of California at San Francisco, San Francisco, CA 94143, U.S.A.

Inhibition of HIV-1 protease by Fmoc-protected N-tosyl arginine derivatives



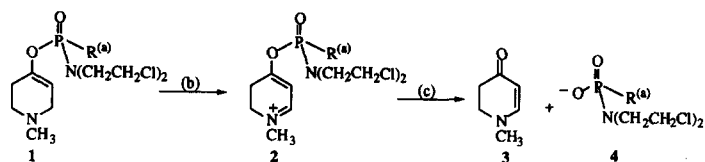
Potential Latent Nitrogen Mustard Derivatives Designed to Target Monoamine Oxidase Rich Cells

Bioorg. Med. Chem. 1997, 5, 1321

You-Xiong Wang and Neal Castagnoli, Jr.*

Department of Chemistry, Virginia Tech, Blacksburg, VA 24061-0212, U.S.A.

(a) $R = \text{NH}_2$ or $\text{NHCH}_2\text{C}_6\text{H}_5$. (b) Allylic α -carbon oxidation of **1** catalyzed by monoamine oxidase A yields the unstable dihydropyridinium **2**. (c) Spontaneous hydrolysis of **2** forms aminoenone **3** and the cytotoxic phosphoramidate mustards **4**.

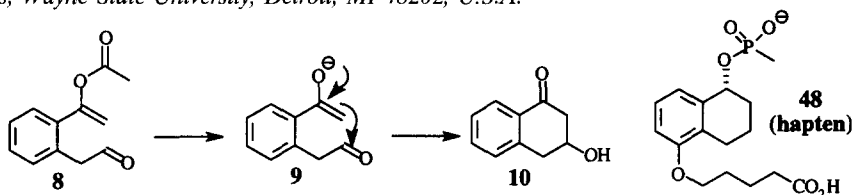


Design and Synthesis of Chiral and Racemic Phosphate-Based Haptens for the Induction of Aldolase Catalytic Antibodies

Bioorg. Med. Chem. 1997, 5, 1327

YongQi Mu and Richard A. Gibbs*

Department of Pharmaceutical Sciences, Wayne State University, Detroit, MI 48202, U.S.A.



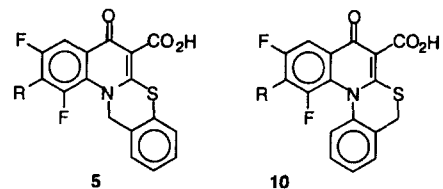
Synthesis and Antibacterial Evaluation of [1,3]Benzo-thiazino[3,2-*a*]quinoline- and [3,1]Benzothiazino[1,2-*a*]quinoline-6-carboxylic Acid Derivatives

Bioorg. Med. Chem. 1997, 5, 1339

Violetta Cecchetti,^a Gabriele Cruciani,^b Enrica Filipponi,^a Arnaldo Fravolini,^{a,*} Oriana Tabarrini^a and Tao Xin^a

^aIstituto di Chimica e Tecnologia del Farmaco and ^bDipartimento di Chimica, Università di Perugia, 06123 Perugia, Italy

A series of [1,3]benzothiazino[3,2-*a*]quinoline (**5**) and [3,1]benzothiazino[1,2-*a*]quinoline-6-carboxylic acids (**10**) were synthesized and evaluated for their in vitro antibacterial activity. The activity was discussed in terms of their structural features revealed by molecular orbital correlation.



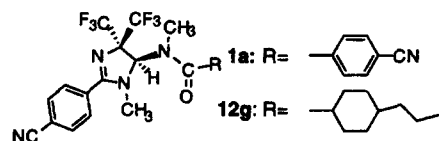
Design, Synthesis, and Structure-Activity Relationship Studies of Novel 4,4-Bis(trifluoromethyl)imidazolines as Acyl-CoA: Cholesterol Acyltransferase (ACAT) Inhibitors and Antihypercholesterolemic Agents

Bioorg. Med. Chem. 1997, 5, 1345

Hui-Yin Li,* Indawati DeLucca, George A. Boswell,* Jeffrey T. Billheimer, Spencer Drummond, Peter J. Gillies and Candy Robinson

The DuPont Merck Pharmaceutical Company, Chemical Sciences Division, Experimental Station, Wilmington, DE 19880-0500, U.S.A.

4,4-Bis(trifluoromethyl)imidazolines were discovered as a novel class of stereospecific and potent orally active ACAT inhibitors. This series of imidazolines may be cholesterol and steroidal mimics.



The Preparation and Bioactivities of (–)-Isovelleral

Bioorg. Med. Chem. 1997, 5, 1363

Mikael Jonassohn,^a Rikard Hjertberg,^a Heidrun Anke,^b
Kim Dekermendjian,^c Arpad Szallasi,^d Eckhard Thines,^b Robin Witt,^c and Olov Sterner^{a,*}

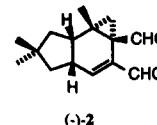
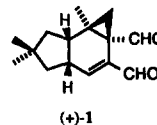
^aDepartment of Organic Chemistry 2, Lund University, Post Office Box 124, S-221 00 Lund, Sweden

^bDepartment of Biotechnology, University of Kaiserslautern, Paul-Ehrlich Straße 23, D-67663 Kaiserslautern, FRG

^cDepartment of Biochemistry, Sct. Hans Hospital, DK-4000 Roskilde, Denmark

^dDepartment of Anatomy and Neurobiology, Washington University School of Medicine, Campus Box 8108, 660 S. Euclid Avenue, St Louis, MO 63110-1093, U.S.A.

The enantiomers of the bioactive fungal sesquiterpene isovelleral (+)-1 and its isomer (–)-2 were prepared, and the bioactivities were compared.



Microbial Biotransformations of a Synthetic Immunomodulating Agent, HR325

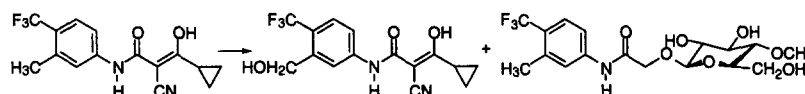
Bioorg. Med. Chem. 1997, 5, 1369

I. Lacroix,^a J. Biton^b and R. Azerad^a

^aLaboratoire de Chimie et Biochimie Pharmacologiques et Toxicologiques, Unité associée au CNRS No. 400, Université René Descartes-Paris V, 45 rue des Saints-Pères, 75270 -Paris Cedex 06, France

^bRoussel Uclaf, Département de Biotechnologie, 102 route de Noisy, 93235 Romainville Cedex, France

Metabolites of HR325 formed in good yields by various fungi have been identified and compared to animal metabolites. An oxidative reaction, which can be mimicked by MCPBA or dimethyldioxirane, is responsible for the cleavage of the cyclopropyl group, resulting in an intermediate cyanohydrin.



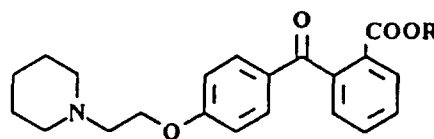
HL 752: A Potent and Long-Acting Antispasmodic Agent

Bioorg. Med. Chem. 1997, 5, 1381

Swati Bal-Tembe,^{*} Dilip N. Bhedi, Anil K. Mishra,
Ramanujam Rajagopalan, Anil V. Ghate, Palakodety Subbarayan, Narayan S. Punekar and
Anjali V. Kulkarni

Research Centre, Hoechst Marion Roussel Ltd., L.B.S. Marg, Mulund, Bombay 400 080, India

From a series of ester analogues, the most potent and long-acting antispasmodic compound, HL 752 (R = isopropyl), was chosen for development.



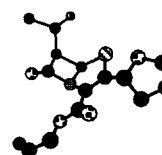
Structure–Activity Relationships of Penem Antibiotics: Crystallographic Structures and Implications for their Antimicrobial Activities

Bioorg. Med. Chem. 1997, 5, 1389

Rie Tanaka,^a Yoshiaki Oyama,^a Seiichi Imajo,^a Shinsuke Matsuki^a and Masaji Ishiguro^{b,*}

^aSuntory Ltd, Institute for Biomedical Research and ^bSuntory Institute for Bioorganic Research, Shimamoto, Osaka 618, Japan

Twelve closely related crystal structures of the penem derivatives revealed a characteristic short S–O contact. The side-chain conformations of the crystal structures showed a good correlation with the antimicrobial activity.



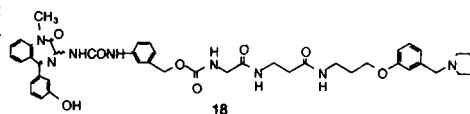
Synthesis and Structure–Activity Relationships of Dual Histamine H₂ and Gastrin Receptor Antagonists with Decreased Hydrophobicity

Bioorg. Med. Chem. **1997**, 5, 1401

Yasuyuki Kawanishi,* Shoichi Ishihara, Tadahiko Tsushima,* Sanji Hagishita, Michio Ishikawa and Yasunobu Ishihara

Shionogi Research Laboratories, Shionogi & Co., Ltd, Fukushima-ku, Osaka 553, Japan

Two types of hybrid compounds either incorporated with a hydrophilic functionality, e.g. hydroxyl (**18**) or a carboxyl, into the molecule or replaced the C₅ phenyl group with a less hydrophobic functionality, e.g. methyl or hydrogen, were synthesized to decrease their high hydrophobicity and evaluated for the dual activities.



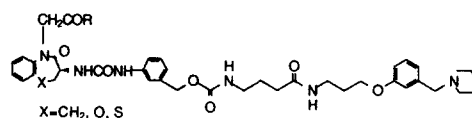
Synthesis and Structure–Activity Relationships of Dual Histamine H₂ and Gastrin Receptor Antagonists with Modified Benzodiazepine Skeletons

Bioorg. Med. Chem. **1997**, 5, 1411

Yasuyuki Kawanishi,* Shoichi Ishihara, Tadahiko Tsushima,* Kaoru Seno, Sanji Hagishita, Michio Ishikawa and Yasunobu Ishihara

Shionogi Research Laboratories, Shionogi & Co., Ltd, Fukushima-ku, Osaka 553, Japan

Dual histamine H₂ and gastrin receptor antagonists with a benzazepine, benzoxazepine, or benzothiazepine moiety as their gastrin receptor antagonist pharmacophores were synthesized and evaluated for the dual activities.



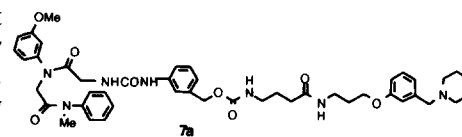
Synthesis and Structure–Activity Relationships of Dual Histamine H₂ and Gastrin Receptor Antagonists with Noncyclic Gastrin Receptor Antagonistic Moieties

Bioorg. Med. Chem. **1997**, 5, 1425

Yasuyuki Kawanishi,* Shoichi Ishihara, Ryuichi Kiyama, Sanji Hagishita, Tadahiko Tsushima,* Michio Ishikawa and Yasunobu Ishihara

Shionogi Research Laboratories, Shionogi & Co., Ltd, Fukushima-ku, Osaka 553, Japan

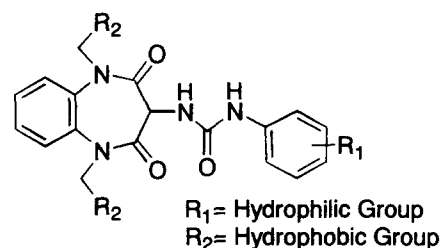
A new type of dual histamine H₂ and gastrin receptor antagonist with a noncyclic dipeptide-type gastrin receptor antagonistic moiety was synthesized and the dual antagonistic activities evaluated. Compound **7a** displayed distinct oral gastric acid antisecretory activities with dose–response relationships for the first time.



Potent and Subtype-Selective CCK-B/gastrin Receptor Antagonists: 2,4-Dioxo-1,5-benzodiazepines with a Plane of Symmetry

Bioorg. Med. Chem. **1997**, 5, 1433

Sanji Hagishita,* Kaoru Seno, Susumu Kamata,* Nobuhiro Haga, Yasunobu Ishihara,* Michio Ishikawa and Mayumi Shimamura
Shionogi Research Laboratories, Shionogi & Co., Ltd, Fukushima-ku Osaka, 553, Japan



Immunostimulatory Activities of Mono- or Diglycosylated α -Galactosylceramides

Bioorg. Med. Chem. 1997, 5, 1447

Akira Uchimura, Toshiyuki Shimizu, Miiko Nakajima, Hitomi Ueno, Kazuhiro Motoki, Hideaki Fukushima, Takenori Natori and Yasuhiko Koezuka*

Pharmaceutical Research Laboratory, Kirin Brewery Co., Ltd, 3 Miyahara-cho, Takasaki-shi, Gunma 370-12, Japan

We examined the effects of 2''- or 3''-monoglycosylated α -GalCers and 2'',3''-diglycosylated α -GalCers on allogeneic MLR and the proliferation of murine spleen cells, and found that their ceramide portions greatly affect their immunostimulatory activities, and that the 3''-hydroxyl group plays a more important role in the immunostimulatory effects of α -GalCer derivatives than the 2''-hydroxyl group.

